REMARKS

Claims 30-34, 47, 61-65, and 72-76 are pending in this application. Claims 30-34, 47, 61-65, and 72-76 are rejected. Claims 35-46, 48-60, 66-71, 77 and 78 have been withdrawn from consideration as being drawn to the non-elected invention. Claim 61 stands objected to. The Applicants herein amend Claims 33, 34, and 61-65. Support for these claims, as amended, can be found in the as-filed claims and specification. Accordingly, these amendments introduce no new matter.

In view of the following amendment and response, the Applicants believe the claims presented herein are allowable. Reconsideration is respectfully requested.

CLAIM TO PRIORITY

The Examiner states that SEQ ID NO:42 was not disclosed in the UK application 9828217.1 Thus she states that the date of 21 December 1999 of PCT/EP99/10297 will be used for purposes of prior art.

For clarification, SEQ ID NO:42 was disclosed in the GB priority document 9828217.1 filed 21 December 1998. Table 3 (p38) of the present application shows the gene encoding SEQ ID NO:42 is SEQ ID NO:41 called bopN. Table 3 of page 28 of the priority document shows the gene sequence encoding bopN as complement of nucleotides 11906-13003. (The fact that it is a complementary sequence is clearly indicated in the table.) The complementary strand presented in the priority document clearly provides all necessary information for determining the coding strand sequence and the encoded amino acid sequence.

CLAIM OBJECTIONS

Claim 61 was objected to because of the wording "...a polypeptide as claimed claim 30..." which was deemed confusing. Amendments were made to claims 61-65 to clarify the purported confusion.

The Applicants respectfully submit that, in view of the forgoing remark, and the claims as amended, the Applicants have overcome these claim rejections. Accordingly, the Applicants respectfully request withdrawal of these rejections.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 30-34, 47, 61-65, and 72-76 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The Examiner states, *inter alia*:

> *The specification fails to identify SEQ ID NO:42 in relation to genes at Table 2 and 3. Further, how are the proteins at page 11, lines 25-30 related to SEQ ID NO:42? What does " ... depending on the particular sequence)." At page 17, line 5 mean in relation to SEQ ID NO:42? How is SEQ ID NO:42 related to the B. pertussis BcrD deduced amino acid sequence at page 35, lines 7-11, and more specifically at Fig. 2? Further, how is SEQ ID NO:42 related to Tables 2 and 3? Further, how is a phage displaying an antibody in a kit used in the production of antibodies at page 25, line 5?*

First, protein of SEQ ID NO:42 can be identified with reference to table 2 and 3. Table 3 gives the nucleic acid sequence corresponding to open reading frames of various named genes. The bopN gene encodes an open reading frame disclosed in SEQ ID NO:41. It is readily apparent from the open sequence given in SEQ ID NO:41 that protein sequence of SEQ ID NO:42 is encoded, thus SEQ ID NO:42 is the polypeptide sequence of the BopN protein.

BopN (SEQ ID NO:42) and BcrD are different proteins. Attention is invited to table 2 for BcrD and table 3 for BopN of pages 37 and 38, respectively. Please note that Table 2 and 3 provide nucleic acid sequences (direct or complementary) to open reading frames of various different genes.

The phage displays an antibody for use in a diagnostic kit on page 25 line 5, and is not used for the preparation of antibodies as alleged by the Examiner.

The Examiner further states

> *...the specification only discloses general concepts of diagnostic assays, antibody, and various kit components that* ***may*** *(emphasis added) provide a diagnostic tool for diagnosing B. pertussis at page 24, line 17-page 25, line 12. Further, the specification only disclose* ***diagnosis*** *(emphasis added) of B. pertussis bacterial infection by assaying infected lung tissue and plating on BG agar, and growth of B. pertussis in liquid culture at page 41, line 27 – page 42, line 6. There also appears to be no working examples of diagnosing B. pertussis using the polypeptide of SEQ ID NO:42.*
>
> *Without further direction or guidance of the exact relevance of SEQ ID NO:42 claimed in the instant invention, how to use the polypeptide of SEQ ID NO:42, working examples disclosing the diagnostic effect(s) of the polypeptide or fragment(s) of SEQ ID NO:42, and antibody production and/or reaction(s) against SEQ ID NO:42, there would be undue experimentation required for one of skill in the art to make and/or use the invention as claimed.*

First, the enablement requirement is satisfied when one skilled in the art, after reading the specification, could practice the claimed invention without undue experimentation. *Ak Steel Corp. v. Sollac,* 344 F.3d 1234, 1244 (Fed.Cir. 2003), citing *In re Wands,* 858 F.2d 731, 736-37 (Fed. Cir. 1988). A specification need not describe -- and best omits – that which is well known in the art. See, e.g. *In re Buchner,* 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991). Further the absence of a working example does not in and of itself compel the conclusion that a specification does not satisfy the requirements of section 112. *In re Long,* 368 F.2d 892, 895, 151 U.S.P.Q. 640, 642 (C.C.P.A. 1966).

As is described in Heuck, C.J. ((1998*) Type III protein secretion systems in Bacterial Pathogens of Animals and Plants. **Microb. Mol. Biol. Rev.*** 62: 379-433 provided as background in the specification on page 5, line 6, a copy of which is provided herewith for the benefit of the Examiner), it was well known before the instant priority filing date that genetic analyses of bacterial virulence factors had shown that pathogens were distinguished from their nonpathogenic relative by presence of specific pathogenicity genes, often organized in so-called pathogenicity islands (clusters of genes). Thus, distantly related pathogens had turned out to harbor closely related virulence genes. This point had become particularly apparent for a set of approximately 20 genes which together encode a pathogenicity mechanism termed type III secretion. Type III secretion enables gram-negative bacterial to secrete and inject pathogenicity proteins into the cytosol of eukaryotic host cells. The type III secretion apparatus is conserved in pathogens as distantly related as *Yersinia* and *Ervinia.*

Although many pertussis virulence associated factors were known such as pertussis toxin, filamentous haemagglutinin, pertactin, which have been included in various acellular vaccines, there have been no convenient genetic method for identifying further virulence factors using the pertussis genome (short of laboriously sequencing the whole genome.) Applicants have now identified genes from the pathogenicity islands which code for type III secretion system thus providing a convenient marker to assess virulence. By providing proteins (or polynucleotides) from the pathogenicity islands, Applicants allowed those within the skilled artisan to detect the presence of virulent Bordetella pertussis without any undue experimentation for diagnostic purposes, such as, by using antibody to pathogenecity proteins of the present invention from blood, urine, saliva tissue biopsy of a patient, as disclosed in page 24 line 17 to page 25 line 6.

Claims 61-65 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states:

The language of the claims is not as precise as the subject matter permits such that one may reasonably know the metes and bounds of the claims and bounds of the claimed subject matter. The claims are indefinite in the recitation of "identifying a polypeptide" and "antibody that is immunospecific for said polypeptide" because it is unclear from the specification what applicant intends. Clarification is required in order to overcome this rejection.

Amendments were made to claims 61-65 which are believed to address the Examiner's ground of rejection.

CLAIM REJECTIONS UNDER 35 U.S.C. § 102(e)

Claims 30-34, 61-65, 72-76 have been rejected under 35 U.S.C. 102(b) as being anticipated by Smith, S. et al. 1996 (J. Clin. Microbiol. 34(2):429-430). Examiner believes that the present proteins are the same as pertussis toxin and filamentous hemagglutinin (FHA) proteins from Bordetella pertussis of Smith et al, and characteristics such as % identity and amino acid sequence would be inherent in the proteins of Smith, S. et al. The Examiner also says that method of Smith, S. et al. and antibody and kit are the same as the instant invention.

The Examiner shifts the burden on Applicants to show a novel or unobvious difference between the claimed proteins and methods with the one in Smith, S. et al.

First, protein of SEQ ID NO:42 is fundamentally different from pertussis toxin (an excreted toxin) and FHA (an adhesion). However, for the convenience of the Examiner the below comparison was conducted.

FHA has accession number in Genpept database as CAD 12824; where as Pertussis Toxin is a multiprotein complex consisting of subunits designated S1 to S5.

Accession number in Genpept database :

- S1 : NP_882282 (length : 269 aa)
- S2 : NP_882283 (length : 226 aa)
- S3 : NP_882286 (length : 227 aa)
- S4 : NP_882284 (length : 152 aa)
- S5 : NP_882285 (length : 133 aa)

The GAP program was used to do each pairwise comparison (using default parameters) of each of the above sequences with SEQ ID NO: 42, and revealed that homology ranged only from about 26% to 29%. It is submitted that instant invention is novel and unobvious from the ones of Smith, S. et al.

Claims 33-33 have been rejected under 35 U.S.C. 102(e) as being anticipated by Rubenfield, M.J. et al. The Examiner states that Rubenfield, M.J. et al. teach an isolated

polypeptide comprising a fragment of 9 amino acids of SEQ ID NO: 29960 with 100% identity to instant SEQ ID NO: 42 amino acids 43-51.

US Patent 6,551,795B1 claims priority to U.S. provisional application Serial No. 60/074,788, filed Feb. 18, 1998 and U.S. provisional application Serial No. 60/094,190 filed Jul. 27, 1998. If U.S. patent or U.S. application publication issues from an application under 35 USC 111(a), the patent or application publication has a 102 (e) prior art date as of the earliest U.S. effective filing date. Effective filing date is the filing date for which priority /benefit is claimed under 35 USC 119(e) and 120 so long as subject matter used to make the rejection is appropriately supported in the earlier filed application's disclosure. In the present case, it is respectfully submitted that Examiner has not shown that the priority documents of US 6,551,795B1 contained an isolated polypeptide comprising an fragment of 9 amino acids of SEQ ID NO;29960. Until such is shown, it is submitted the rejection under 102(e) is improper.

The Applicants reserve the right to prosecute, in one or more patent applications, the claims to non-elected inventions, the claims as originally filed, and any other claims supported by the specification. The Applicants thank the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration and allowance of the pending claims is earnestly solicited. If it would expedite the prosecution of this application, the Examiner is invited to confer with the Applicants' undersigned attorney.

Respectfully submitted,

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